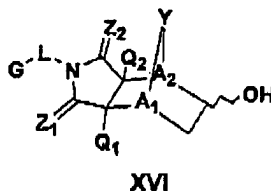


In re Application of Salvati et al.,  
 S.N. 10/024,878  
 Filed: 12/19/2001  
 Attorney Docket No. LD0297CIP  
 Response to First Office Action

# CLAIM AMENDMENTS:

1. (CURRENTLY AMENDED) A method for preparation of a compound of the following formula XVI, or salt thereof:



where

G is an aryl or heterocyclo group, where said group is mono- or polycyclic, and which is optionally substituted at one or more positions;

Z<sub>1</sub> is O or S; [, S, NH, or NR<sup>6</sup>];

Z<sub>2</sub> is O or S; [, S, NH, or NR<sup>6</sup>];

A<sub>1</sub> is CR<sup>7</sup> [or N];

A<sub>2</sub> is CR<sup>7</sup> [or N];

Y is J-J'-J'' where J is (CR<sup>7</sup>R<sup>7'</sup>)<sub>n</sub> and n = 0-3, J' is O, S, S=O, SO<sub>2</sub>, NH, NR<sup>7</sup>, OP=OOR<sup>2</sup>, OC=O, NR<sup>1</sup>C=O, OP=ONHR<sup>2</sup>, OSO<sub>2</sub>, NHNH, NHR<sup>8</sup>, NR<sup>6</sup>NH, or N=N, and J'' is (CR<sup>7</sup>R<sup>7'</sup>)<sub>n</sub> and n = 0-3;

Q<sub>1</sub> is H, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocycloalkyl or substituted heterocycloalkyl, arylalkyl or substituted arylalkyl, alkynyl or substituted alkynyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo, halo, CN, R<sup>1</sup>OC=O, R<sup>4</sup>C=O, R<sup>5</sup>R<sup>6</sup>NC=O, HO-CR<sup>7</sup>R<sup>7'</sup>, nitro, R<sup>1</sup>OCH<sub>2</sub>, R<sup>1</sup>O, NH<sub>2</sub>, C=OSR<sup>1</sup>, SO<sub>2</sub>R<sup>1</sup> or NR<sup>4</sup>R<sup>5</sup>;

Q<sub>2</sub> is H, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocycloalkyl or substituted heterocycloalkyl, arylalkyl or substituted arylalkyl, alkynyl or substituted alkynyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo, halo, CN, R<sup>1</sup>OC=O, R<sup>4</sup>C=O, R<sup>5</sup>R<sup>6</sup>NC=O, HO-CR<sup>7</sup>R<sup>7'</sup>, nitro, R<sup>1</sup>OCH<sub>2</sub>, R<sup>1</sup>O, NH<sub>2</sub>, C=OSR<sup>1</sup>, SO<sub>2</sub>R<sup>1</sup> or NR<sup>4</sup>R<sup>5</sup>;

L is a bond, (CR<sup>7</sup>R<sup>7'</sup>)<sub>n</sub>, NH, NR<sup>8</sup> or NR<sup>5</sup>(CR<sup>7</sup>R<sup>7'</sup>)<sub>n</sub>, where n = 0-3;

R<sup>1</sup> and R<sup>1'</sup> are each independently H, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocyclo or substituted heterocyclo, cycloalkylalkyl or

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substituted cycloalkylalkyl, cycloalkenylalkyl or substituted cycloalkenylalkyl, heterocycloalkyl or substituted heterocycloalkyl, aryl or substituted aryl, arylalkyl or substituted arylalkyl;

R<sup>2</sup> is alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocyclo or substituted heterocyclo, cycloalkylalkyl or substituted cycloalkylalkyl, cycloalkenylalkyl or substituted cycloalkenylalkyl, heterocycloalkyl or substituted heterocycloalkyl, aryl or substituted aryl, arylalkyl or substituted arylalkyl;

R<sup>4</sup> is H, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocyclo or substituted heterocyclo, cycloalkylalkyl or substituted cycloalkylalkyl, cycloalkenylalkyl or substituted cycloalkenylalkyl, heterocycloalkyl or substituted heterocycloalkyl, aryl or substituted aryl, arylalkyl or substituted arylalkyl, R<sup>1</sup>C=O, R<sup>1</sup>NHC=O, SO<sub>2</sub>OR<sup>1</sup>, or SO<sub>2</sub>NR<sup>1</sup>R<sup>1'</sup>;

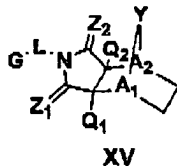
R<sup>5</sup> is alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocyclo or substituted heterocyclo, cycloalkylalkyl or substituted cycloalkylalkyl, cycloalkenylalkyl or substituted cycloalkenylalkyl, heterocycloalkyl or substituted heterocycloalkyl, aryl or substituted aryl, arylalkyl or substituted arylalkyl, R<sup>1</sup>C=O, R<sup>1</sup>NHC=O, SO<sub>2</sub>R<sup>1</sup>, SO<sub>2</sub>OR<sup>1</sup>, or SO<sub>2</sub>NR<sup>1</sup>R<sup>1'</sup>;

R<sup>6</sup> is alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocyclo or substituted heterocyclo, cycloalkylalkyl or substituted cycloalkylalkyl, cycloalkenylalkyl or substituted cycloalkenylalkyl, heterocycloalkyl or substituted heterocycloalkyl, aryl or substituted aryl, arylalkyl or substituted arylalkyl, CN, OH, OR<sup>1</sup>, R<sup>1</sup>C=O, R<sup>1</sup>NHC=O, SO<sub>2</sub>R<sup>1</sup>, SO<sub>2</sub>OR<sup>1</sup>, or SO<sub>2</sub>NR<sup>1</sup>R<sup>1'</sup>; and

R<sup>7</sup> and R<sup>7'</sup> are each independently H, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocyclo or substituted heterocyclo, cycloalkylalkyl or substituted cycloalkylalkyl, cycloalkenylalkyl or substituted cycloalkenylalkyl, heterocycloalkyl or substituted heterocycloalkyl, aryl or substituted aryl, arylalkyl or substituted arylalkyl, halo, CN, OR<sup>1</sup>, nitro, hydroxylamine, hydroxylamide, amino, NHR<sup>4</sup>, NR<sup>2</sup>R<sup>5</sup>, NOR<sup>1</sup>, thiol, alkylthio or substituted alkylthio, R<sup>1</sup>C=O, R<sup>1</sup>(C=O)O, R<sup>1</sup>OC=O, R<sup>1</sup>NHC=O, SO<sub>2</sub>R<sup>1</sup>, SOR<sup>1</sup>, PO<sub>3</sub>R<sup>1</sup>R<sup>1'</sup>, R<sup>1</sup>R<sup>1'</sup>NC=O, C=OSR<sup>1</sup>, SO<sub>2</sub>R<sup>1</sup>, SO<sub>2</sub>OR<sup>1</sup>, or SO<sub>2</sub>NR<sup>1</sup>R<sup>1'</sup>;

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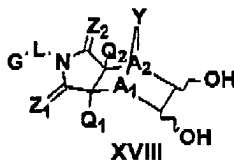
comprising the steps of contacting a compound of the following formula XV, or salt thereof:



where the symbols are as defined above;

with an enzyme or microorganism capable of catalyzing the hydroxylation of said compound XV to said compound XVI, and effecting said hydroxylation.

2. (WITHDRAWN) A method for preparation of a compound of the following formula XVIII, or salt thereof:



where

G is an aryl or heterocyclo group, where said group is mono- or polycyclic, and which is optionally substituted at one or more positions;

Z<sub>1</sub> is O, S, NH, or NR<sup>6</sup>;

Z<sub>2</sub> is O, S, NH, or NR<sup>6</sup>;

A<sub>1</sub> is CR<sup>7</sup> or N;

A<sub>2</sub> is CR<sup>7</sup> or N;

Y is J-J'-J'' where J is (CR<sup>7</sup>R<sup>7'</sup>)<sub>n</sub> and n = 0-3, J' is O, S, S=O, SO<sub>2</sub>, NH, NR<sup>7</sup>, OP=OOR<sup>2</sup>, OC=O, NR<sup>1</sup>C=O, OP=ONHR<sup>2</sup>, OSO<sub>2</sub>, NHNH, NHNR<sup>6</sup>, NR<sup>6</sup>NH, or N=N, and J'' is (CR<sup>7</sup>R<sup>7'</sup>)<sub>n</sub> and n = 0-3;

Q<sub>1</sub> is H, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocycloalkyl or substituted heterocycloalkyl, arylalkyl or substituted arylalkyl, alkynyl or substituted alkynyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo, halo, CN, R<sup>1</sup>OC=O, R<sup>4</sup>C=O, R<sup>5</sup>R<sup>6</sup>NC=O, HOCR<sup>7</sup>R<sup>7'</sup>, nitro, R<sup>1</sup>OCH<sub>2</sub>, R<sup>1</sup>O, NH<sub>2</sub>, C=OSR<sup>1</sup>, SO<sub>2</sub>R<sup>1</sup> or NR<sup>4</sup>R<sup>5</sup>;

Q<sub>2</sub> is H, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocycloalkyl or substituted

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heterocycloalkyl, arylalkyl or substituted arylalkyl, alkynyl or substituted alkynyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo, halo, CN,  $R^1OC=O$ ,  $R^4C=O$ ,  $R^5R^6NC=O$ ,  $HO-CR^7R^8$ , nitro,  $R^1OCH_2$ ,  $R^1O$ ,  $NH_2$ ,  $C=OSR^1$ ,  $SO_2R^1$  or  $NR^4R^5$ ;

L is a bond,  $(CR^7R^8)_n$ , NH,  $NR^5$  or  $NR^5(CR^7R^8)_n$ , where  $n = 0-3$ ;

$R^1$  and  $R^1'$  are each independently H, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocyclo or substituted heterocyclo, cycloalkylalkyl or substituted cycloalkylalkyl, cycloalkenylalkyl or substituted cycloalkenylalkyl, heterocycloalkyl or substituted heterocycloalkyl, aryl or substituted aryl, arylalkyl or substituted arylalkyl;

$R^2$  is alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocyclo or substituted heterocyclo, cycloalkylalkyl or substituted cycloalkylalkyl, cycloalkenylalkyl or substituted cycloalkenylalkyl, heterocycloalkyl or substituted heterocycloalkyl, aryl or substituted aryl, arylalkyl or substituted arylalkyl;

$R^4$  is H, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocyclo or substituted heterocyclo, cycloalkylalkyl or substituted cycloalkylalkyl, cycloalkenylalkyl or substituted cycloalkenylalkyl, heterocycloalkyl or substituted heterocycloalkyl, aryl or substituted aryl, arylalkyl or substituted arylalkyl,  $R^1C=O$ ,  $R^1NHC=O$ ,  $SO_2OR^1$ , or  $SO_2NR^1R^1'$ ;

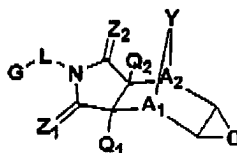
$R^5$  is alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocyclo or substituted heterocyclo, cycloalkylalkyl or substituted cycloalkylalkyl, cycloalkenylalkyl or substituted cycloalkenylalkyl, heterocycloalkyl or substituted heterocycloalkyl, aryl or substituted aryl, arylalkyl or substituted arylalkyl,  $R^1C=O$ ,  $R^1NHC=O$ ,  $SO_2R^1$ ,  $SO_2OR^1$ , or  $SO_2NR^1R^1'$ ;

$R^6$  is alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocyclo or substituted heterocyclo, cycloalkylalkyl or substituted cycloalkylalkyl, cycloalkenylalkyl or substituted cycloalkenylalkyl, heterocycloalkyl or substituted heterocycloalkyl, aryl or substituted aryl, arylalkyl or substituted arylalkyl, CN, OH,  $OR^1$ ,  $R^1C=O$ ,  $R^1NHC=O$ ,  $SO_2R^1$ ,  $SO_2OR^1$ , or  $SO_2NR^1R^1'$ ; and

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$R^7$  and  $R^7$  are each independently H, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocyclo or substituted heterocyclo, cycloalkylalkyl or substituted cycloalkylalkyl, cycloalkenylalkyl or substituted cycloalkenylalkyl, heterocycloalkyl or substituted heterocycloalkyl, aryl or substituted aryl, arylalkyl or substituted arylalkyl, halo, CN,  $OR^1$ , nitro, hydroxylamine, hydroxylamide, amino,  $NHR^4$ ,  $NR^2R^5$ ,  $NOR^1$ , thiol, alkylthio or substituted alkylthio,  $R^1C=O$ ,  $R^1(C=O)O$ ,  $R^1OC=O$ ,  $R^1NHC=O$ ,  $SO_2R^1$ ,  $SOR^1$ ,  $PO_3R^1R^1$ ,  $R^1R^1NC=O$ ,  $C=OSR^1$ ,  $SO_2R^1$ ,  $SO_2OR^1$ , or  $SO_2NR^1R^1$ ;

comprising the steps of contacting a compound of the following formula XVII, or salt thereof:



XVII

where the symbols are as defined above;

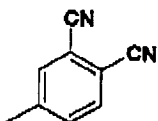
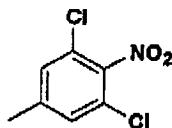
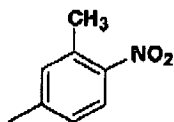
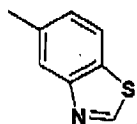
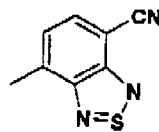
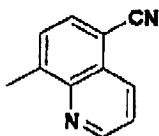
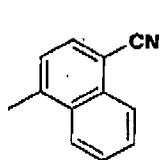
with an enzyme or microorganism capable of catalyzing the opening of the epoxide ring of compound XVII to form the diol of said compound XVIII, and effecting said ring opening and diol formation.

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3. (ORIGINAL) The method of claim 1 wherein a microorganism is incubated with the compound of formula XV to effect the hydroxylation.

4. (ORIGINAL) The method of claim 1 wherein the reaction mixture, after hydroxylation, is separated by chiral HPLC.

5. (NEW) The method of claim 1 wherein R<sup>7</sup> is alkyl or substituted alkyl; L is a bond; and G is selected from the group consisting of:



and

